Amendments to the Specification

Please amend paragraph [0256] appearing on pages 124-125 of the specification as follows:

Examples of high throughput instrumentation which can be used according to the present invention are well known in the art. Non-limiting examples of such instruments include ImageTrak® (Packard BioScience), the FLIPR® system, ~~Spectramax~~ SPECTRAMAX® Gemini or FMax (Molecular Devices Corporation, Sunnyvale, CA), VIPR™ II Reader (Aurora Biosciences Corporation, San Diego, Ca), Fluoroskan II (GMI, Inc., Albertville, MN), ~~Fluoroskan Ascent~~ FLUOROSKAN ASCENT® (Labsystems, Franklin, MA), ~~Cytofluor~~ CYTOFLUOR® or ~~Cytofluor~~ CYTOFLUOR® 4000 (Perkin Elmer Instruments), ~~Cytofluor~~ CYTOFLUOR® 2300 (Millipore, FLx800TBID, FLx800TBIDE, ELx808, ELx800, FL600 (Bio-Tek Instruments), Spectrafluora, Spectrofluora Plus, Ultra or Polarion (Tecan AG), MFX (Dynex Technologies, Chantilly, VA), Fluoro Count (Packard Instruments Co.), NOVOstar, POLARstar Galaxy or FLUOstar Galaxy (BMG Lab Technologies GmbH), Fluorolite 1000 (Dynex Technologies), 1420 Victor 2 (EG&G Wallac, Inc., also available through PerkinElmer), and Twinkle LB 970 (Berthold Technologies GmbH & Co.).

Please amend paragraph [0304] appearing on page 154 of the specification as follows:

30 mg of Jurkat lysate was mixed with 100 µL Protein A SEPHAROSE® ~~Sepharose~~ beads (Zymed) which had been washed 2 times with 1 mL PBS and incubated at 4 °C for 2 hours. The mix was centrifuged 1 minute at 2,700 x g. The supernatant was removed from the Protein A SEPHAROSE® ~~Sepharose~~ beads and 50 µg of rabbit anti-FITC antibody (Zymed) was added. Lysates and antibody were incubated with gentle rocking at 4 °C for 2 hours. 100 µL pre-washed Protein A SEPHAROSE® ~~Sepharose~~ beads were added to the mix and further incubated overnight, with gentle rocking at 4 °C. The SEPHAROSE® ~~Sepharose~~ beads were collected by centrifugation (2,700 x g, 1 minute) and washed 6 times with 1 mL of PBS + 0.2 % NP-40. 100 µL of 2x SDS

sample buffer (Invitrogen Corporation) with 40 mM dithiothreitol (DTT) was added to the beads and the beads were boiled at 100 °C for 5 minutes. Samples were spun down at 20,000 x g for 1 minute and the supernatant removed and loaded onto 6 mm wide wells on a 16 cm x 20 cm x 1 mm 4 % SDS polyacrylamide gel in Tris-glycine running buffer (Invitrogen Corporation) and run at 35 mA for 4 hours at room temperature. The gel was removed from the glass plate and stained with 1 % coomassie blue in 40 % methanol, 7.5 % acetic acid overnight at room temperature. The gel was destained in a solution of 40 % methanol, 7.5 % acetic acid with several changes of solution until protein bands were visible. Stained bands were excised with a clean razor blade and stored in microfuge tubes for tryptic digest.

Please amend paragraph [0320] appearing on page 161 of the specification as follows:

Human transferrin receptor and caspase 8 siRNA oligos were chemically synthesized by Ambion (Austin, TX). The target sequence for the transferrin receptor siRNA was 5' AAC TTC AAG GTT TCT GCC AGC 3' (nucleotides 1480-1497 of SEQ ID NO.: 27) and for caspase 8 was 5' AAG GAA AGT TGG ACA TCC TGA 3'(SEQ ID NO.: 40). The control siRNA oligos, human cyclophilin and negative control scrambled siRNA were also from Ambion. 293T cells were grown to 50% confluence and allowed to attach overnight. siRNAs were transfected into the cells using Lipofectamine 2000 (Invitrogen, Carlsbad, CA) according to the manufacturer's instructions. Briefly, siRNA (at a final concentration of 50 nM) and lipid were individually diluted in low serum media, ~~Opti-MEM~~ OPTI-MEM® (Invitrogen, Carlsbad, CA) and allowed to incubate for 10-30 min after which they were combined and allowed to form lipid complexes for 20 min. The lipid complexes were added onto the cells and allowed to incubate for 48h. The cells were then harvested for RNA, protein, FACS analysis, or DAPI staining.

Please amend paragraph [0321] appearing on page 162 of the specification as follows:

For cDNA synthesis and quantitative PCR, total RNA was extracted using the ~~TRIzol~~ TRIzol® reagent (Invitrogen, Carlsbad, CA) according to the manufacturer's instructions. Total RNA was quantitated, denatured, and electrophoresed in an agarose-formaldehyde gel to determine integrity of total RNA. 2 μg of total RNA was then used to make cDNA by reverse transcription using the ~~Retroscript~~ RETROSCRIPT® cDNA synthesis kit (Ambion Austin, TX) according to the manufacturer's instructions. Both oligo dT and random primers were used to make the cDNA which was used as a template for PCR analysis. Quantitative PCR was done by Sybrgreen incorporation using the Quantitect kit (Qiagen, Valencia, CA) on the ~~LightCycler~~ LIGHTCYCLER® (Roche Molecular Biochemicals, Mannheim, Germany) using standard conditions. Data was normalized against the housekeeping gene, cyclophyllin. The cells transfected with cyclophilin as a control was normalized against glyceraldehyde phosphate dehydrogenase (GAPD).

Please amend paragraph [0324] appearing on page 163 of the specification as follows:

For the immunoprecipitation, 1 mg of Jurkat lysate was pre-cleared with 50μl Protein A SEPHAROSE® ~~Sepharose~~ (Zymed Laboratories, San Francisco, CA). Lysates were then incubated with 2.5μg of rabbit anti-FITC antibody (Zymed Laboratories, San Francisco, CA) for 2 h at 4°C. Lysates and antibody were then added to 100ul pre-washed Protein A SEPHAROSE® ~~Sepharose~~ and incubated overnight at 4°C. SEPHAROSE® ~~Sepharose~~ was washed six times with RIPA. 20% of the above immunoprecipitation was subjected to SDS-PAGE and transferred to PVDF. Membranes were blocked in 3% milk, 1% BSA and probed with anti-transferrin receptor antibody (Zymed) as decribed above.

Please amend paragraph [0326] appearing on pages 163-164 of the specification as follows:

96-well plates were coated with soluble human transferrin receptor (shTR) (Merck Biosciences, Schwalbach, Germany) at 375 ng/well and blocked with Bovine Serum Albumin (BSA). Wells were incubated with increasing concentrations of biotin-GA in binding/washing buffer containing 0.5 % BSA, 0.1% Tween®-20 ~~Tween-20~~, 150 mM NaCl and 10 mM Tris-HCl (pH 7.4) for 1 hour at room temperature. Wells were washed 4 times, incubated with Eu-Streptavidin (Perkin-Elmer, Wellesey, MA) and washed again. Amounts of bound Eu-Streptavidin were quantified after incubation with Enhancement Solution (Perkin-Elmer, Wellesey, MA) by measuring time-delayed fluorescence on a Wallac Victor plate reader (Perkin-Elmer, Wellesey, MA) according to manufacturer's protocol. Uncoated wells were used to determine background binding. Biotinylated inactive GA (biotin-α,β saturated GA) was used as a control and produced only low background signal in both coated and uncoated wells. In competition experiments biotin-GA at 1 μM was pre-mixed with increasing amounts of GA or inactive-GA. K_d and competition EC_{50} values were calculated using PRIZM software. ShTR-coated wells were incubated with GA-biotin as described above, washed and incubated with non-tagged analogs or binding/washing buffer as a wash off control. Separate control wells were probed with biotinylated holo-transferrin (bio-Trn) to control for TR retention and possible denaturation over long incubation times.

Please amend paragraph [0337] appearing on pages 168-169 of the specification as follows:

Protein concentration of the lysate was determined by DC Assay (BioRad). 30 mgs of Jurkat lysate was mixed with 100 μL Protein A ~~Sepharose~~ SEPHAROSE® beads (Zymed) which had been washed 2 times with 1 ml PBS and incubated at 4° C for 2 hours. The mix was centrifuged 1 minute at 2,700 x g. The supernatant was removed from the Protein A ~~Sepharose~~ SEPHAROSE® beads and 50 μg of rabbit anti-FITC antibody (Zymed) was added. Lysates and antibody were incubated with gentle rocking

at 4°C for 2 hours. 100 µL pre-washed Protein A ~~Sepharose~~ SEPHAROSE® beads were added to the mix and further incubated overnight, with gentle rocking at 4°C. The ~~Sepharose~~ SEPHAROSE® beads were collected by centrifugation (2,700 x g, 1 minute) and washed 6 times with 1 ml of PBS + 0.2% NP-40. 100 µL of 2x SDS sample buffer (Invitrogen Corporation) with 40 mM dithiothreitol (DTT) was added to the beads and the beads were boiled at 100°C for 5 minutes. Samples were spun down at 20,000 x g for 1 min and the supernatant removed and loaded onto 6 mm wide well on a 16 cm x 20 cm x 1 mm 4% SDS polyacrylamide gel in Tris-glycine running buffer (Invitrogen Corporation) and run at 35 mA for 4 hours at room temperature. The gel was removed from the glass plate and stained with 1% coomassie blue in 40% methanol, 7.5% acetic acid overnight at room temperature. The gel was destained in a solution of 40% methanol, 7.5% acetic acid with several changes of solution until protein bands were visible. Stained bands were excised with a clean razor blade and stored in microfuge tubes for tryptic digest.

Please amend paragraph [0342], appearing on page 173 of the specification as follows:

Protein concentration of the lysate was determined by DC Assay (BioRad). 30 mgs of Jurkat lysate was mixed with 100 µL Protein A SEPHAROSE® ~~Sepharose~~ beads (Zymed) which had been washed 2 times with 1 ml PBS and incubated at 4° C for 2 hours. The mix was centrifuged 1 minute at 2,700 x g. The supernatant was removed from the Protein A SEPHAROSE® ~~Sepharose~~ beads and 50 µg of rabbit anti-FITC antibody (Zymed) was added. Lysates and antibody were incubated with gentle rocking at 4°C for 2 hours. 100 µL pre-washed Protein A SEPHAROSE® ~~Sepharose~~ beads were added to the mix and further incubated overnight, with gentle rocking at 4°C. The SEPHAROSE® ~~Sepharose~~ beads were collected by centrifugation (2,700 x g, 1 minute) and washed 6 times with 1 ml of PBS + 0.2% NP-40. 100 µL of 2x SDS sample buffer (Invitrogen Corporation) with 40 mM dithiothreitol (DTT) was added to the beads and the beads were boiled at 100°C for 5 minutes. Samples were spun down at 20,000 x g for 1 min and the supernatant removed and loaded onto 6 mm wide well on a 16 cm x 20 cm

x 1 mm 4% SDS polyacrylamide gel in Tris-glycine running buffer (Invitrogen Corporation) and run at 35 mA for 4 hours at room temperature. The gel was removed from the glass plate and stained with 1% coomassie blue in 40% methanol, 7.5% acetic acid overnight at room temperature. The gel was destained in a solution of 40% methanol, 7.5% acetic acid with several changes of solution until protein bands were visible. Stained bands were excised with a clean razor blade and stored in microfuge tubes for tryptic digest.